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Evaluation of serum interleukin-17 and tumour necrosis factor-α levels in patients with vitiligo

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ABSTRACT

Background: According to definitions, vitiligo is an acquired cutaneous complicated condition caused by functional melanocyte loss in the epidermis. It is characterised by milky white macules of diverse sizes and shapes that have a tendency to grow peripherally over time. Cytokines play a critical role in the depigmentation process of vitiligo and control the immune response and inflammation.

Objective: The present study aimed to estimate the serum levels of pro-inflammatory cytokines, interleukin 17, and tumour necrosis factor alpha in vitiligo patients and healthy subjects.

Materials and Methods: In order to conduct the study, samples from 60 patients were collected and samples from 60 healthy participants (the control group) were pooled and measured using sandwich ELISA. Data on the patient's age, sex, family history, disease state, stress exposure, and males smoking are collected as part of the study.

Results: Patients with vitiligo had higher levels of IL-17 (73.23 pg/mL ± 14.85 pg/mL versus 5.79 pg/mL ± 1.53 pg/mL) and also increased levels of TNF-α (186.82 pg/mL ± 57.31 pg/mL versus 44.19 pg/mL ± 5.95 pg/mL) compared to controls. The present results show significant difference of IL-17 levels between active disease state and stable disease state (p=0.007). But the present results show non-significant difference of IL-17 levels according to sex (p=0.257), family history (p=0.924), smoking (p=0.878) and exposure to stress (p=0.971). The mean levels of TNF-α was lower in male patients with smoking in comparison with patients without smoking, and the difference was significant (p=0.031). But the present results show non-significant difference of TNF-α levels according to family history (p=0.910), disease state (p=0.196) and exposure to stress (p=0.940).

Conclusion: The present study suggests that IL-17 and TNF-α were strongly associated with autoimmune vitiligo and may play a crucial role in the condition's development and severity

Key words: vitiligo , IL-17 (Interleukin-17) , TNF-α (Tumor Necrosis Factor- α)

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INTRODUCTION

A inherited loss of pigment is vitiligo following destruction of epidermal melanocytes [1], which leads to appearance of milky white macules and patches that are seen clinically [2]. Vitiligo is a multifactorial polygenic disease. Four theories could explain its pathogenesis: auto-cytotoxicity, antioxidant theory, neural theory, and autoimmune theory [3]. Of which, the autoimmune theory is the most important one, in which various cytokines and inflammatory mediators play a major role [4].

Numerous immune-mediated disorders have been linked to the pathophysiology of the cytokine interleukin-17. If interleukin-17 contributes to the vitiligo, an autoimmune pigmentary skin condition [4]. In this study, we combine genetic information from vitiligo patients to show that interleukin-17 may be a key player in the etiology of the disease. This has ramifications for developing novel biomarkers as well as how we understand the biology of vitiligo.

A pro-inflammatory cytokine known as Tumor Necrosis Factor (TNF), which is at the root of many autoimmune illnesses, has been linked to the depigmentation process in vitiligo. We examine its function in vitiligo by examining its pro-inflammatory characteristics [5].

MATERIALS AND METHODS

The following research groups were the subjects of a case-control study at that time from November 2022 to the end of February 2023. In the present investigation's patient group of 60, with ages ranging from 15 years to 40 years, there were 24 males and 36 females. This investigation was conducted at Al-Sader City Hospital Medical in Al-Najaf, Iraq. Physician as vitiligo diagnosed the patients clinically. Patients were interviewed directly by using an anonymous questionnaire form that age, sex , family history, disease state, males smoking and exposure to stress. This study also included 22 males and 38 females as a control group 60 presumably healthy individuals. All participants provided informed consent in accordance with the ethical committee of Al-Najaf health department. This study was subjected to evaluate IL-17 and TNF-α by ELISA technique, three millilitres of blood were transferred to a sterile Gel tube using disposable syringes, permitted to coagulate at ambient temperature, followed by centrifugation at 2500 revolutions per minute for ten minutes. The serum was then placed in Eppendorf containers and frozen at -20°C for future use.

RESULTS

Serum levels of Interleukin 17 (IL-17)

Mean levels of serum IL-10 were 73.23 pg/mL ± 14.85 pg/mL and 5.79 pg/ml ± 1.53 pg/ml in patients with vitiligo and healthy control respectively; the level was highly significant lower in patients with vitiligo in comparison with healthy control (p<0.001). The present results show significant difference of IL-17 levels between active disease state and stable disease state 76.85 pg/mL ± 15.41 pg/mL and 66.01 pg/ml ± 10.72 pg/ml respectively (p=0.007). But the present results show non-significant difference of IL-17 levels according to sex (p=0.257), family history (p=0.924), msles smoking (p=0.878) and exposure to stress (p=0.971). These results were presented in the Table 1.

Serum levels of Tumor Necrosis Factor Alpha (TNF-α)

Mean levels of serum IL-10 were 186.82 pg/ml ± 57.31 pg/ml and 44.19 pg/ml ± 5.95 pg/ml in patients with vitiligo and healthy control respectively; the level was highly significant lower in patients with vitiligo in comparison with healthy control (p<0.001). The present results show significant difference of TNF-α levels between female and male, 198.70 pg/ml ± 58.05 pg/ml and 169.0 pg/ml ± 52.03 pg/ml respectively, (p= 0.048). Mean levels of serum TNF-α were 148.62 pg/ml ± 45.99 pg/ml and 192.69 pg/ml ± 56.97 pg/ml in male patients with smoking and patients without smoking respectively; the mean levels was lower in patients with smoking in comparison with patients without smoking, and the difference was significant (p=0.031). But the present results show non-significant difference of TNF-α levels according to family history (p=0.910), disease state (p=0.196) and exposure to stress (p=0.940). These results were presented in the Table 1.

DISCUSSION

Several human studies have investigated the roles that IL-17 play a role in vitiligo. The present results show the mean levels of serum IL-17 were 73.23 pg/ml ± 14.85 pg/ml and 5.79 pg/ml ± 1.53 pg/ml in patients with vitiligo and healthy control respectively; the level was highly significant higher in patients with vitiligo in comparison with healthy control (p<0.001). Consistence with the present results Yasmin et al [6], show abundance of these IL-17 producing cells was increased in vitiligo relative to control subjects (p=0.001). The current findings support previous research by Khan et al [7], that found a significantly higher level of IL17 in vitiligo sufferers compared to healthy controls. The elevated level of IL17 found in this study supported the theory that the development of vitiligo may be caused by a shift in the immune system toward Th1 or Th17 and away from Tregs and Th2. It is tempting to hypothesize that Th17 cells and Tregs exist in a balance such that in the absence of Tregs, Th17 activity amplifies inflammatory cascades that involve the skin of patients with vitiligo [8]. Th17 cells, which are more prevalent in the serum of individuals with active vitiligo, are the major source of IL-17 cytokines. Although these findings show that IL-17 is involved in vitiligo, its function appears to be less important than that of other cytokines. By causing monocyte cells to produce additional pro-inflammatory cytokines including TNF-α, IL-1, and IL-6, IL-17 may aid in the maintenance of the inflammatory network [9]. Interleukin-17 is able to induce the release of pro-inflammatory cytokines such as IL-1, IL-6, TNF α, TGFβ. These cytokines recruit and activate lymphocytes or neutrophils, which are involved in vitiligo pathogenesis and may cause further inhibition of melanocyte proliferation. In vitro human cultured melanocytes treated with IL-17 displayed a reduced melanin production [6]. Singh et al, [10] noted an approximately 30% decrease in melanin production from IL-17-treated melanocytes (p<0.05). Furthermore, IL-17 was observed to cause morphological

Tab. 1. Frequency distribution of IL-17 and TNF-α in serum of Vitiligo patients and controls

Characteristic	IL-17	TNF-α
Study groups		
Vitiligo patients	73.23 ± 4.85	186.82 ± 57.31
Controls	5.79 ± 1.53	44.19 ± 5.95
p value	< 0.001	< 0.001
Sex		
Male	75.91 ± 16.63	169.0 ± 52.03
Female	71.45 ± 13.49	198.70 ± 58.05
P value	0.257	0.048
Disease status		
Active	76.85 ± 15.41	193.63 ± 61.41
Stable	66.01 ± 10.72	173.20 ± 46.53
P value	0.007	0.196
Family history		
Positive	72.49 ± 15.46	188.17 ± 62.42
Negative	73.53 ± 14.79	186.28 ± 55.91
P value	0.924	0.91
Exposure to stress		
Positive	73.34 ± 17.74	185.95 ± 64.10
Negative	73.19 ± 13.67	187.19 ± 54.93
P value	0.971	0.94
Males smoking		
Positive	74.00 ± 16.17	148.62 ± 45.99
Negative	73.11 ± 14.80	192.69 ± 56.97
P value	0.878	0.032

shrinking of melanocytes, further contributing to decreased pigment production. The present results show the mean levels of serum IL-17 were 76.85 pg/mL ± 15.41 pg/mL and 66.01 pg/ml ± 10.72 pg/ml in patients with active state, and patients with stable state respectively; the mean levels was higher in patients with active state in comparison with patients with stable state, and the difference was significant (p=0.007).

According to the current study, vitiligo patients' blood levels of TNF- α were substantially higher than those of healthy controls. TNF- α plays a key effector role in the immunopathological processes underlying vitiligo since its main role in the disease is the modulation of immune responses. TNF-α promotes keratinocyte apoptosis, which sets off an autoimmune reaction and results in the death of melanocytes [11]. Many studies have reported an increase in TNF-α levels in patients with vitiligo compared with the control group, thereby supporting the present finding [11-13]. Nevertheless, several studies also claimed that there was no appreciable distinction in cytokine levels between the patient and control groups [14]. Yu et al [15], have discovered that people with vitiligo had lower blood levels of TNF- α. Anti-TNF drugs can cure vitiligo, although the effectiveness of the therapy varies, and some individuals who use anti-TNF medications for other conditions have also developed vitiligo [5]. The present results found non-significant correlation between TNF-α level and disease activity (p=0.196), family history (p=0.910) and exposure to stress (p=0.940). It has been established that tumor necrosis factor-a functions in both innate and adaptive immunity in addition to being cytotoxic for some tumor cells. Increased TNF-α may change melanocyte activities such as immunologic cytotoxicity susceptibility, differentiation, and proliferation. By lowering the intracellular levels of tyrosinase and tyrosinase-related protein1, TNF-α may prevent melanogenesis [16]. Additionally, as keratinocytes play a role in maintaining the homeostasis of melanocytes, any alteration to keratinocytes may result in melanocyte malfunction. High TNF-α levels may contribute to keratinocyte death, which reduces the generation of melanogenic cytokines and, consequently, the loss of melanocytes. TNF-α is therefore viewed as a complicated mediator that controls melanocyte apoptosis [17].

CONCLUSION

The current review of the literature leads to the conclusion that IL-17 is strongly associated with autoimmune vitiligo and may play a crucial role in the condition's development and severity. Human investigations have shown that vitiligo patients had higher blood IL-17 levels and more circulating Th17 cells. TNF-α levels in vitiligo have been the subject of inconsistent results in recent investigations. The results of the current investigation point to TNF-α as a potential player in the vitiligo lesion formation; however, the exact nature of this function is not entirely clear.

AUTHOR'S CONTRIBUTIONS

BE Conceptualized the study, designed the research methodology, collected, and analyzed data. AM drafted the initial version of the manuscript. All authors critically reviewed and revised the manuscript for intellectual content. All authors read and approved the final version for submission.

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